Editorial

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Therapy for Amblyopia: A newer perspective

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Amblyopia is a reduction of best-corrected visual acuity that cannot be contributed to the structural abnormality of the eye. The prevalence of amblyopia is between 2% and 5%.[1] Amblyopia is associated most commonly with early childhood strabismus and anisometropia and less commonly with ametropia and vision deprivation such as congenital cataract.

The conventional treatments for amblyopia include refractive correction, occlusion, and atropine penalization. Optimal refractive correction alone can resolve in at least one-third of cases with untreated anisometropic amblyopia and even some untreated strabismic amblyopia.[2] If amblyopia is not resolved, occlusion or pharmacological penalization with atropine on the better eye is often prescribed simultaneously or soon after refractive correction is provided.

Even with spectacle correction plus occlusion or atropine penalization, there are still one-third of amblyopia have poor response to treatment. Eyes with poor initial visual acuity, the presence of significant astigmatism, and age of over 6 years are risk factors of treatment failure.[3] Compliance with amblyopia treatments has a major effect on response to therapy.

Compliance of conventional amblyopic treatment is generally low. Discomfort from eye patches, difficulties with vision from occluding the better eye, psychological distress, uncomfortable effect of bright sunlight to the atropine-treated eye, and ocular sensitivity to atropine are the causes of poor compliance.[4]

Reduced Connectivity between Brain Areas

Recent studies have shown that the physiological basis of amblyopia is mainly located at visual cortex and lateral geniculate nucleus. Functional magnetic resonance imaging study in human amblyopia suggests that V1 may be the earliest anatomic site in the visual pathway.[5,6] Optimized voxel-based morphometry indicates that human amblyopes have reduced gray matter volume in visual cortical region.[7] Amblyopic deficit not only involves circumscribed visual areas as visual cortex and lateral geniculate nucleus but also reduced the effective connectivity in different visual areas.[8] The effective connectivity loss was found correlated with the degree of amblyopia. Feedforward and feedback connectivities are similarly affected.

Plasticity of Visual System

The effect of treatment for amblyopia usually decreases after critical period which is thought to be 6 years of age and is thought attributing to decreased brain plasticity.

The plasticity of visual system is greatest in early infancy. It is triggered by maturation of inhibitory, gamma-aminobutyric acid (GABA)-producing interneurons.[9] In amblyopes, there is suppression from the better-seeing eye over the amblyopic eye.[10] GABA is thought to play a key role in suppression of inputs from the amblyopic eye within the visual cortex.

The Role of Suppression in Amblyopia

Early concept think that suppression simply

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follows amblyopia. Treatments of amblyopia focus on occlusion or penalization of the better eye because the input from the amblyopic eye is weaker. The treatment does not concern suppression. The current concept thinks that suppression plays the causal role in amblyopia. Disruption of binocular function causes suppression leading to amblyopia.

Using dichoptic motion coherence threshold technique,[11] quantitative measurement of interocular suppression is assessed in strabismic and anisometropic amblyopia. It is found that deeper suppression is associated with poorer vision in the amblyopic eye.

Due to limited success of conventional treatment for amblyopia and the new concept of brain plasticity, a variety of treatment strategies were investigated. These include dichoptic treatments and pharmacological therapy.

Dichoptic Treatment

Suppressive interactions within the visual cortex are a viable target for amblyopia treatment. Theory of dichoptic training bases on the concept that the binocular circuitry from the weak amblyopic eye is actively suppressed by the strong fellow eye.[12] Dichoptic training tasks reduce fellow eye contrast to rebalance the contrast between the eyes. Dichoptic treatment of amblyopia promotes binocular vision and reduces inhibitory interactions within the visual cortex. Reduce suppression within the visual cortex was found enhancing improvements in binocular visual function in adult amblyopes. Repeated exposures to dichoptic motion coherence threshold stimuli effectively reduce suppression in adults with amblyopia, which in turn improve visual acuity and stereopsis. These visual improvements are sustained and have so far been demonstrated in adults well beyond the critical period of visual development.

Behavioral treatments including perceptual learning, dichoptic training, and video game are found improving visual function in adult amblyopia. A meta-analysis found that these new methods yielded a mean improvement of visual acuity of 0.17 logMAR with 32% of patients achieving gains $\geq$0.2 logMAR.[13]

Although dichoptic amblyopic therapy shows significant visual improvement in children and adult amblyopic patient, there is no home-based dichoptic training design and most of the training needs a supervisor.[14] No long-term comparison of conventional occlusion treatment and dichoptic treatment has been studied. Design of home-based dichoptic amblyopic treatment with long-term randomized control trial needs further investigation.

Pharmacological Treatment

In this issue, Singh *et al*. reviewed studies on pharmacological therapy for amblyopia. The drugs in this review include levodopa-carbidopa combination and antidepressants such as fluoxetine, GABA antagonists, and cytidine 5′-diphosphocholine (choline or citicoline).

The effect of levodopa was studied on many aspects. It can increase endogenous expression of nerve growth factor, increase expression of N-methyl-D-aspartate receptor-1-subunit in visual cortical neurons which is reduced in amblyopia, improve visual evoked potential response, increase visual acuity, and decrease fixation point scotomas.

Chronic administration of fluoxetine promotes the recovery of visual functions in adult amblyopic animals by reducing the intracortical inhibition and increasing the expression of brain-derived neurotrophic factor in the visual cortex.

GABA antagonist was found able to restore binocularity. However, it also has serious adverse effect. Significant visual improvement was found in citicoline administration.

However, most of these drugs are still in experimental stage. Further evaluations of efficacy and side effect of these drugs are needed.

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